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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,435	05/19/1999	HANS CARLSSON	1103326-0560	6135

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	20

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/308,435	Applicant(s) Carlsson et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with th c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 13, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-37 and 45-60* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 9-16, 19-37, 45-53, 55, and 58-60* is/are rejected.

7) ☒ Claim(s) *8, 17, 18, 54, 56, and 57* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 38, 39-44 have been canceled.

New Claims 53-60 have been submitted.

Claims 1-37, 45-60 are pending and under consideration..

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2003 has been entered

Allowable Subject Matter

3. Claims 8, 17-18, 54, 56-57 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or reasonably suggest the incorporation of a chaotropic agent in to a polymer particle that comprises a water insoluble protein antigen.

Objections and Rejections Withdrawn

4. Claims 50-52 objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim must not depend from another multiple dependent claim and must depend from a prior claim in the alternative, in light of the amendment of the claims to depend from prior claims in the alternative and not to depend from another multiple dependent claim.

5. Claim 1 rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al (1998),number 6, paragraph 14, and in view of a certified English translation of the Swedish priority document having been received prior to the filing of the instant RCE.

6. Claims 38, 49,58-60 rejected under 35 U.S.C. 102(b) as being anticipated by Bolin et al (WO96/38475), in light of the guidance incorporated by reference to Rabinovich et al (Bolin et al page 11, lines 8-15, which teaches microcapsules vary in composition and size but are between 5 and 10 m (see Rabinovich (Science) page 6, of 15, paragraph 4, Rabinovich et al reference provided herewith, micrometers), in light of the cancellation of claim 38.

7. Claims 38, 49, 58-60 rejected under 35 U.S.C. 102(b) as being anticipated by Michael et al (US Pat. 5,629,001) in light of the cancellation of claim 38.

8. Claims 1, 2-10, 19-22, 24-25, 37-38, 45-49, 53-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the cancellation of claim 38, the amendment of the other claims to clearly provide antecedent basis for the recited claim limitations and the addition of clarifying statements in other claims.

Objections and Rejections Maintained

9. Claims 1 (claims 58-60 dependent claims 49, 37 and 1), 37, 45-49, 50 (dependent upon claim 37), 51-52 (depend from amended claim 50), 58-60 directed to a composition and methods of use are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the a method of making polymer particles that comprise a protein or lipoprotein, does not reasonably provide enablement for vaccines comprising any protein from any source or any Helicobacter protein from any species or any fragment of any Helicobacter protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

10. Claims 1, 26-27, 36 (fragment thereof) rejected under 35 U.S.C. 102(b) as being anticipated by Goldstein et al (1997) for reasons of record in paper number 6, paragraph 15, and in light of claim amendments submitted May 2001.

11. Claims 1-3,6-7, 9, 11-14 rejected under 35 U.S.C. 102(b) as being anticipated by Fountain et al (US Pat. 4,610,868) for reasons of record in paper number 6, paragraph 16.

12. Claims 1, 3-6, 9, 12, 19-20, 23-25, 32-37,45-48, 49,50 (newly amended), 58 are rejected under 35 U.S.C. 102(b) as being anticipated by WO96/36317 (reference made of record in Applicant's 1449).

13. Claims 1,2-4, 11-13, 19-23, 32-37,45-48, 49,50 (newly amended), 53, 55, 58 are rejected under 35 U.S.C. 102(b) as being anticipated by WO95/11009 (reference made of record in Applicant's 1449).

14. Claims 1, 2-4, 11-13, 19-23, 32-37,45-48, 49,50 (newly amended), 53, 55, 58 are rejected under 35 U.S.C. 102(b) as being anticipated by WO95/11010 (reference made of record in Applicant's 1449).

15. Claims 1, 26-31, 37, 51-52 (newly amended) are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolin (reference of record) in light of Rabinovich et al, in view of WO96/36317 (reference made of record in Applicant's 1449).

16. Claims 1, 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO96/36317 (reference made of record in Applicant's 1449) in view of Weers et al (US Pat. 6,309,623).

Response to Arguments

17. The rejection of claims 1 (claims 58-60 dependent claims 49, 37 and 1), 37, 45-49, 50, 51-52 (claims 51-52 administer a composition for treatment, preventing or reducing risk of H.pylori infection), 58-60 (new claims) rejected under 35 U.S.C. 112, first paragraph (scope) is traversed on the grounds that "[T]he Examiner appears to have lost sight of the fact that the invention is not directed to vaccines per se."

18. Clearly the Examiner has not lost sight of the fact that Applicant is claiming compositions that must function as vaccines based upon the claimed methods of preventing or treating pre-existing infection.

It is the position of the examiner that the instantly claimed compositions are used in claimed methods of treatment (claims 51 and 59) and methods of preventing or reducing the risk

of Helicobacter infection (claims 52, and 60). The methods administer a composition. The methods therefore administer a composition that comprise any Helicobacter insoluble protein antigen or fragment thereof. The composition claims have been amended to no longer recite the word "vaccine" but are used in the methods treatment and preventing infection; the compositions are no longer required to function as vaccines. The claims are only enabled for a scope of the claimed invention. The combination of Helicobacter HpaA together with cholera toxin goes to the heart of the claimed inventions that are directed to methods of treating, preventing or reducing risk of infection. The critical components needed for induction of a protective immune response are not claimed. Therefore, Applicant's compositions which are used in methods of treatment, and preventing infection must function as a vaccine.

At no time did the examiner state that Applicant was not enabled for a scope of the claimed method of making a delivery system, but compositions that are made by a specific process (claim 37) that must function to provide treatment, prevention or reducing risk of infection (claims 45-49, 50-52, 58-60), are not enabled for the full scope of the claimed invention, as all Helicobacter insoluble proteins and Helicobacter insoluble protein fragments will not serve to provide treatment, prevention or reduction of risk of infection by Helicobacter as compositions that comprise Helicobacter proteins do not predictably produce the desired positive effect (see paper number 6, paragraph 11; response to arguments in paper number 14, paragraph 17).

Monath et al (1994) showed parenteral administration of an H.pylori antigen induced a strong serum IgG response but was unprotective. Laszlo et al (1992, English translation) showed a H.pylori antigenic composition that induced a serious allergic negative side effect in a patient, and no protection against Helicobacter infection.

Additionally, at present there are more than 20 different species of Helicobacter known in the art (acinoyx; bilis; bizzozero; canis; chlorum; cholecystus; cinadei; coli; colifelis; felis; felix; fenelliae; heilmannii; hepaticus; jejuni; maninz; mesocricetus; muetelae; muridarium; mustalae; nemstrinae; oedipus; pametensis; pullorum;pylori; rappini; rodentium; salmonii; sputorum; suncus;

trogontum; and upsaliensis) and the instant specification has not described insoluble Helicobacter proteins from all of these species which are able to treat, prevent or reduce Helicobacter infection. Of the known species of Helicobacter, the genome of Helicobacter pylori has been sequenced (Tomb et al, August 1997, Nature), and about 15,000 open reading frames for bacterial proteins were found. Each species of Helicobacter therefore represents a large number of protein antigens. Applicant has not taught which of 1000's of Helicobacter proteins that would be insoluble Helicobacter protein antigens could or would serve to induce protection against infection. Any and all compositions, that comprise an insoluble Helicobacter antigen or fragment thereof, would not predictably function in the claimed methods of treatment, preventing or reducing risk of infection in light of the cited prior art that provides evidence that Helicobacter antigens do not predictably function to induce a protective immune response against infection, especially in light of how many potential protein antigens that are produced by the more than 20 species of Helicobacter known in the art.

19. Applicant asserts that the claimed invention is only directed to means of delivering a water insoluble antigen.

20. It is the position of the examiner that Applicant claims are directed to:

a. methods of making delivery systems,

b.compositions that comprise a delivery system that contains an insoluble protein antigen,

c. compositions that comprise a delivery system that contains an insoluble protein antigen that is a Helicobacter protein antigen or fragments thereof; and

d. methods of treating and preventing Helicobacter infection.

21. The rejection of claims 1, 26-27, 36 (fragment thereof) under 35 U.S.C. 102(b) as being anticipated by Goldstein et al (1997) is traversed on the grounds "it is unclear to Applicant's how claim 36 found its way into this rejection."

22. It is the position of the examiner that the ratio of the water phase to the oil phase is based upon a volume to volume ratio. For example on page 24, sections 2.2.4, 25 ml of organic phase (O), DMF, was combined with 25 ml of water. This ratio is 1:1 based upon a volume to volume ratio. This is one reason why claim 36 was included in this rejection. Claim 36 recites a range of O to W ratios that Goldstein et al disclosed.

23. Applicant asserts that "It is inherent in the setting out of the steps that the steps are to be carried out in the order given, unless some language is added to specify otherwise."

24. It is the position of the examiner that the claimed methods, recite "comprising" language which permits the methods steps to be carried out in any order, such as: step a) followed by step b); step a) and step b) carried out simultaneously; and step b) followed by step a).

25. Applicant additional traverses the Application of Goldstein et al against claims 1, 26-27 and 36 on the grounds that "the Examiner has had to bring in a completely different reference, that of Murray, as the basis for this assertion".

26. It is the position of the examiner that the rejection of the claims over Goldstein et al was based upon inherency (see paper number 6, paragraph 15). Murray was provided as evidence that protein fragments function as antigens. Murray was not the basis of the rejection of the claims. Goldstein et al inherently anticipates the instantly claimed invention. It is the position of the examiner that Goldstein et al anticipate claims 1, 26-27 and 36 and not all of the pending claims.

27. With respect to the application of the Goldstein et al, the phrase "Helicobacter protein fragment" is asserted as requiring the fragment to be at least a portion of the intact protein that is recognizable as being derived from said intact protein.

28. It is the position of the examiner that what is claimed is an antigenic fragment of a Helicobacter protein. An antigen is a molecule that is so defined by the antibody that binds thereto. The antigenic fragment of a Helicobacter protein is not size limited to any specific

portion or sequence of amino acids, but must be a fragment that reacts with an antibody. Epitopes are portions of a whole protein, and in light of Murray, a single amino acid can function as an antigenic epitope; epitopes are also known to be fragments of 3 to 10 amino acids. The antigenic fragments recited in the claims are not defined to immunoreact with any specific antibody and can be a single amino acid in light of Murray et al. Applicant's arguments are not commensurate in scope with the instantly claimed invention.

29. At page 20, paragraph 3, the Goldstein et al reference is additionally traversed on the grounds that "the Examiner appears to have lost sight of the purport of the instant invention. The Examiner is reminded that, in the claims in question, Applicants are not claiming a method of immunizing."

30. It is the position of the examiner that with respect to the Goldstein et al reference, no immunizing methods steps were argued in paper number 7, page 7, paragraph 22. Why Applicant discusses the scope of enablement rejection over the claimed methods of treatment, preventing and reducing Helicobacter infection, when Goldstein et al was only applied against composition claims, points to the fact that Applicant appears to have lost sight of the claims to which Goldstein et al was applied.

31. Applicant states " [I]n other words, the Examiner's stance with respect to claims 17 and 18 is effectively an acknowledgment that the allegation of non-enablement of claim 1 and claims dependent therefrom is without merit.

32. Contrary to Applicant's assertion that the Examiner's stance that claims 17 and 18 define enablement for compositions used in the claimed methods (claims 50, 51-52, 58-60 which depend from claims 1, 37, 45-49) of treatment, preventing and reducing risk of Helicobacter infection is incorrect. Claims 17 and 18 have do not recite any claim limitations directed to Helicobacter pylori. Claim 37 does not depend from claims 17 or 18. Arguments directed to the scope of

enablement rejection are addressed above. Claims 17 and 18 are free of the prior art of record and contain allowable subject matter.

33. The rejection of claims 1-3, 6-7, 9, 11-14 under 35 U.S.C. 102(b) as being anticipated by Fountain et al (US Pat. 4,610,868) is traversed on the grounds that Applicant's invention is directed to a process of preparing compositions.

34. It is the position of the examiner that Fountain et al disclose and claims methods of making a delivery system; the embodiment disclosed in Fountain et al meeting the claim limitations which recite the steps of:

Claims 1: a) **mixing**:

i. an aqueous phase (see Fountain et al, claim 50, col. 20, line 34),

ii.one or more solubilizing agents (see claims 67-68, surfactant),

iii. a matrix polymer/organic solvent and a stabilizing agent (see claim 50, lines 31-33 and 39).

b) **forming droplets** (forming globular structures, see claim 50) col. 20, line 40) and removing the solvent (see claim 51, col. 20, lines 44-45; see col. 22, claim 101) and thereby incorporating the water insoluble protein (hydrophobic compound, see claim 50, col. 20, lines 32-33 and col. 22, claims 81-85, claim 94).

Instant claim 2: more than one stabilizing agent (see claim 50 and claim 67);

Instant claim 3: stabilizing agent is a polymer, polar lipids and hydrophobic surfactant (see claims 56-60 and 67-68);

Instant claim 6: non-ionic hydrophobic surfactant (see col. 6, line 44; claim 68);

Instant claim 7: utilizes alkylslphate salt (see Fountain, col. 6, line 41);

Instant claim 9: sorbitan fatty acid ester (see col. 6, lines 34-56, and claim 68).

Instant claims 11-14 (see col. 6, lines 40, 44, claim 50 together with claims 67-68). Fountain et al anticipates the instantly claimed invention for reasons of record.

35. The rejection of claims 1, 3-6, 9, 12, 19-20, 23-25, 32-38,45-48, 49, 58 rejected under 35 U.S.C. 102(b) as being anticipated by WO96/36317 (reference made of record in Applicant's 1449) is traversed on the grounds that the reference "does not disclose mixing an aqueous phase with a water insoluble protein."

36. It is the position of the examiner that WO96/36317 does disclose the step of **mixing** an aqueous phase (see page 19, Table 1) with a water insoluble protein (see page 20, lines 25-36 and page 21, lines 1-2; specifically page 21, lines 10-11)and one or more solubilizing agents (see page 22, lines 25-30) with an organic phase/ polymer (see page 12, lines 3-30 for list of polymers; page 13, lines 4-5) to produce an emulsion. Table 1 discloses water as an aqueous phase that is mixed with an organic phase (acetone) and a matrix polymer (poly-vinyl-alcohol) which is used in the formulation of a delivery system that incorporates an insoluble protein.

37. Applicant asserts that the "reference does not disclose mixing an aqueous phase with a water-insoluble protein."

38. It is the position of the examiner that the polymer solution defined in Table 1, page 19 that discloses water as part of the mixture, is an aqueous phase to which an active agent, insoluble protein is added (see page 20, lines 21-36 and page 22).

forming droplets of emulsion through dispersing (see page 24, line 22) the emulsion in a fluid medium (see page 25, lines 13-19); and

removing the organic non-solvent (see page 17, lines 1-37 (non-solvent is defined to be the organic solvent); page 11, lines 10-11 extraction vessel, page 25, line 33 from the emulsion droplets (see page 25, line 10)to obtain polymer particles (see page 25, lines 20-22) having water insoluble protein antigen incorporated therein (see page 17, lines 4-9 (non-solvent is the organic phage); page 3, lines 27-29). The reference teaches the utilization of stabilizers together with solubility (see page 22, lines 25-31), surfactants (see page 22, lines 14-17) and bulking agents (see page 22, lines 3-31). A three phase flow of gas, liquefied gas and frozen micro droplets defines a

relationship of W/O/X (see page 15, lines 1-37 and page 16). An additional embodiment disclosed comprise the utilization of a spray atomizer which directs the flow of liquid gas which freezes the emulsion providing means for subsequent extraction of solvent solutions to form micro particles (see page 7, lines 33-37 and top of page 8 and page 9, lines 5-10) as well as metal cations (see page 22, lines 35-37) and a pore forming agent (see page 23, lines 6-13). The polymers are homogenous or mixtures of polymers (see page 12, lines 3-37 and page 13, lines 1-10). The ration of the polymer to solvent (aqueous phage) is from 5% to 20% which corresponds to 1:5 or 5:100 (see page 13, lines 10-15). The particles produced are 1 micrometer (see page 9, line 26). The reference inherently anticipates the now claimed invention.

39. Applicant points to page 21, of the applied WO96' document and states that the reference does not teach the claimed invention as steroids are not hydrophobic proteins.
40. The examiner agrees, that steroids are not proteins, but page 21 was cited for teaching the incorporation of hydrophobic molecules into the disclosed delivery system. At page 21, lines 1-2, vitamins are exemplified as a protein for incorporation into the delivery system; vitamins are known hydrophobic protein molecules. The reference anticipates the instantly claimed invention.

41. The rejection of claims 1,2-4, 11-13, 19-23, 32-38,45-48, 49, 50, 53, 55, 58 under 35 U.S.C. 102(b) as being anticipated by WO95/11009 (reference made of record in Applicant's 1449) is traversed on the grounds that the reference does not disclose mixing an aqueous phase with a water insoluble protein.
42. It is the position of the examiner that WO95/11009 disclose a method of producing a vaccine delivery system, the method comprising the steps of: **mixing** an aqueous phase (see figures, PVA in water, excess water, especially Figure 2) with a water insoluble protein (see WO95', page 3, lines 19-23, and claims 14, 15, 24 (growth hormone is a hydrophobic protein: see US Pat. 6013773, see col.1, lines 25-40 and Table 2, col. 3, lines 5-18) and 25 (gp120 is also known to

comprise a hydrophobic loop); and one or more solubilizing agents (see page 5, lines 19-24) with an organic phase/ polymer (see page 4, lines 3-6 for organic phase; page 3, lines 14-18 for list of polymers;) to produce an emulsion.

43. Applicant asserts that the antigens of WO95' are not the antigens of the instantly claimed invention which are water insoluble proteins.

44. It is the position of the examiner that WO95' discloses the incorporation of (see claims), growth hormone or gp120 into the delivery system. Growth Hormone is known to be an insoluble protein, considered to evidence a very low solubility (see evidence provided in Kobayashi et al, US Pat. 6,013,773, col. 1, lines 25-40 and Table 1 for growth hormone). WO95' discloses water insoluble proteins for incorporation into a delivery system, the insoluble proteins comprising hydrophobic characteristics. The reference inherently anticipates the now claimed invention for reasons of record in paper number 14.

45. The rejection of claims 1, 2-4, 11-13, 19-23, 32-38,45-48, 49, 50, 53, 55, 58 are rejected under 35 U.S.C. 102(b) as being anticipated by WO95/11010 (reference made of record in Applicant's 1449) is traversed on the grounds that the reference does not "disclose mixing an aqueous phase with a water insoluble protein".

46. It is the position of the examiner that the reference does disclose a mixing step that comprises mixing water/aqueous phase, an organic phase, an insoluble protein (a drug), the drug being an antigen of choice. Among the antigens disclosed for incorporation into the delivery system are antigens (WO95/11010, page 12, lines 29-38) such as gp160 (see US Pat.6,569,418, which provides evidence that gp160 is a membrane bound hydrophobic antigen, see 6569418, key-word in context paragraph provided Detailed Description text paragraph 222), and Nef (see USPat 6197583, which teaches Nef to comprise hydrophobic and polar residues, Figures 3 and 8), both antigens that possess hydrophobic character, and thus are inherently insoluble antigens. The words used to describe the antigens of WO95' are not the same as Applicant's, but among the

disclosed antigens for incorporation into the delivery system of WO95' are insoluble antigens; the reference anticipates the instantly claimed invention for reasons of record.

47. The rejection of claims 1, 26-31, 37, 51-52 (newly amended), as previously applied to claims 1, 26-31 under 35 U.S.C. 103(a) as being unpatentable over Bolin (reference of record) in light of Rabinovich et al, in view of WO96/36317 (reference made of record in Applicant's 1449), is traversed on the grounds that WO96' "does not teach water-insoluble antigens in the context of W/O emulsion technology".

48. It is the position of the examiner that Bolin et al in light of Rabinovich et al, in view of WO96' teaches the claimed invention. Bolin et al in light of Rabinovich et al teach, suggest and provide guidance for the incorporation of an Helicobacter pylori lipoprotein (insoluble antigen) into a polymer delivery system; the method steps of making the delivery system (micro particles) not being fully described. WO96/36317 produces polymer matrixes containing polymer particles that comprise a protein antigen with lower losses of biologically active agent, high product yields and is able to produce the polymer matrix containing polymer particles at the commercial scale (see WO96/36317 :page 1, lines 21-24). Among the antigens described by WO96' are vitamins, vitamins being known to include hydrophobic insoluble proteins, thus teaching the delivery system of WO96' to be compatible with both hydrophobic and hydrophilic protein antigens.WO96/36317 provides clear and methodical steps for the attainment of the desired polymer matrix delivery system in high product yields through the utilization of the combination of aqueous and organic solvent solutions that contain solubilizers and stabilized to attain the desired result (see discussion of WO96/36317 above). In the absence of a showing of unexpected results, Bolin in light of Rabinovich in view of WO96/36317 obviate the now claimed invention.

49. The rejection of claims 1, 15-16 under 35 U.S.C. 103(a) as being unpatentable over WO96/36317 (reference made of record in Applicant's 1449) in view of Weers et al (US Pat. 6,309,623) is traversed on the grounds that WO96' does not "water insoluble protein antigens".

50. It is the position of the examiner that WO96/36317 does teach the incorporation of antigens into the delivery system that are hydrophobic (vitamins include hydrophobic proteins) in nature. The word "insoluble" in not recited in the WO96' document, but among the antigens described, for incorporation into the delivery system, are hydrophobic, insoluble antigens. Therefore, both WO96' and Weers et al are analogous art; both WO96' and Weers teaching the utilization of surfactants and Weers defining a specific species of cationic surfactant that is combinable with a protein antigen. The rejection is maintained for reasons of record.

51. USPat. 6,514,523 is cited to show the utilization of carrier particles that incorporate a apolipoprotein therein.

52. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242. The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp May 19, 2003

L. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600